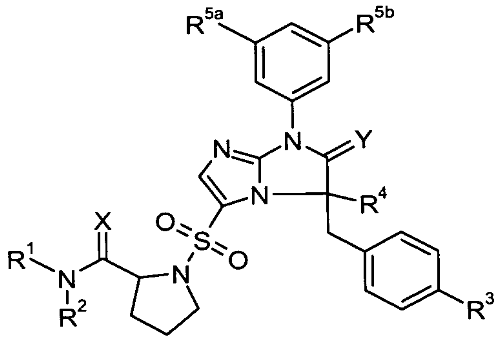
CLAIMS

We Claim:

1. A compound of the formula I:



(I),

wherein:

R^1 and R^2 are each independently selected from the group consisting of:

(A) hydrogen, with the proviso that R^1 and R^2 are not both hydrogen atoms;

(B) $-R^{100}$, which is:

a straight or branched alkyl of 1 to 7 carbon atoms or cycloalkyl of 3 to 6 carbon atoms, which alkyl or cycloalkyl group is mono- or poly substituted with moieties independently selected from the group consisting of:

(i) oxo,

(ii) cyano,

(iii) halogen,

(iv) moieties of the formula $-COOR^6$, wherein R^6 is a hydrogen atom, a straight or branched alkyl of 1 to 7 carbon atoms or cycloalkyl of 3 to 6 carbon atoms,

(v) moieties of the formula $-OR^7$, wherein R^7 is a hydrogen atom, a straight or branched alkyl group of 1 to 7 carbon atoms or an acyl group of the formula $-COR^8$ wherein R^8 is a straight or branched alkyl group of 1 to 7 carbon atoms,

- (vi) moieties of the formula $-NR^9R^{10}$, wherein R^9 and R^{10} are each, independently selected from the group consisting of:
  - (a) hydrogen,
  - (b) straight or branched alkyl of 1 to 7 carbon atoms,
  - (c) acyl of the formula $-COR^{11}$ wherein R^{11} is a straight or branched alkyl group of 1 to 7 carbon atoms, and
  - (d) groups of the formula $-COOR^{12}$ wherein R^{12} is a straight or branched alkyl group of 1 to 7 carbon atoms,

  or wherein R^9 and R^{10} constitute a bridge consisting of 3-5 methylene groups or 2-4 methylene groups and one oxygen atom, such that the groups R^9 and R^{10} together with the nitrogen atom between them form a heterocyclic ring,
- (vii) saturated heterocyclic groups, consisting of 3 to 5 methylene groups and one oxygen atom, wherein said heterocyclic groups are optionally mono- or disubstituted with moieties that are independently selected from the group consisting of:
  - (a) oxo and
  - (b) straight or branched alkyl of 1 to 3 carbon atoms; and
- (viii) aryl, selected from the group consisting of:
  - (a) furyl,
  - (b) tetrazolyl and
  - (c) thiophenyl;

(C) aryl, selected form the group consisting of:

- (i) biphenyl,
- (ii) phenyl which is mono- or di-substituted with moieties independently selected from the group consisting of $-NH_2$ and N-morpholino, and
- (iii) quinolinyl; and

(D) unsaturated or partially saturated heterocyclic groups consisting of 2 to 3 carbon atoms, 1 to 2 nitrogen atoms, 0 to 1 sulfur atoms and 0 to 1 oxygen atoms wherein said heterocyclic group is optionally mono- or polysubstituted with one or more of the following moieties independently selected from the group consisting of:

(i) oxo and

(ii) straight or branched alkyl of 1 to 7 carbon atoms;

or wherein R^1 and R^2 constitute a saturated 3 to 5 methylene group bridge which together with the nitrogen atom between them form a heterocyclic ring, wherein said heterocyclic ring is mono- or disubstituted with moieties independently selected from the group consisting of:

(A) -OH,

(B) –COOH and

(C) -$CONH_2$;

R^3 is:

(A) aryl selected from the group consisting of pyridyl and pyrimidyl, wherein one or more hydrogen atoms of said aryl group are optionally and independently substituted with moieties selected from the group consisting of:

(i) cyano,

(ii) halogen and

(iii) groups of the formula $-NR^{13}R^{14}$, wherein R^{13} and R^{14} are each, independently, hydrogen or straight or branched alkyl of 1 to 3 carbon atoms;

(B) trifluoromethoxy or,

(C) cyano;

R^4 is straight or branched alkyl of 1 to 3 carbon atoms;

R^{5a} is Cl or CF_3;

R^{5b} is Cl or CF_3;

X is an oxygen or a sulfur atom; and

Y is an oxygen or a sulfur atom;

or a pharmaceutically acceptable salt thereof.

2. A compound of formula I according to claim 1, wherein:

R^1 and R^2 are each independently selected from the group consisting of:

- (A) hydrogen with the proviso that R^1 and R^2 are not both hydrogen atoms;
- (B) $-R^{100}$, which is:

  a straight or branched alkyl of 1 to 4 carbon atoms, which alkyl group is mono- or disubstituted with moieties independently selected from the group consisting of:

  - (i) oxo,
  - (ii) OH,
  - (iii) moieties of the formula $-NR^9R^{10}$, wherein R^9 and R^{10} are each, independently selected from a group consisting of:
    - (a) hydrogen and
    - (b) methyl,
  - (iv) tetrazole,

or wherein R^1 and R^2 constitute a saturated 5 methylene group bridge which together with the nitrogen atom between them form a heterocyclic ring, wherein said heterocyclic ring is monosubstituted with COOH;

R^3 is:

- (A) aryl selected from the group consisting of 3-pyridyl and 5-pyrimidyl wherein said aryl group is monosubstituted with:
  - (i) cyano or
  - (ii) NH_2,
- (B) trifluoromethoxy or
- (C) cyano;

R^4 is a methyl group;

R^{5a} is Cl;

R^{5b} is Cl;

X is an oxygen atom and

Y is an oxygen atom;

or a pharmaceutically acceptable salt thereof.

3. A compound of formula I according to claim 1, wherein:

R^1 and R^2 are each independently selected from the group consisting of:

(A) hydrogen with the proviso that R^1 and R^2 are not both hydrogen atoms, or

(B) $-R^{100}$, which is:

straight or branched alkyl of 1 to 4 carbon atoms, which alkyl group is mono- or disubstituted with moieties independently selected from the group consisting of:

(i) oxo,

(ii) OH and

(iii) NH_2;

R^3 is trifluoromethoxy or cyano;

R^4 is a methyl group;

R^{5a} is Cl;

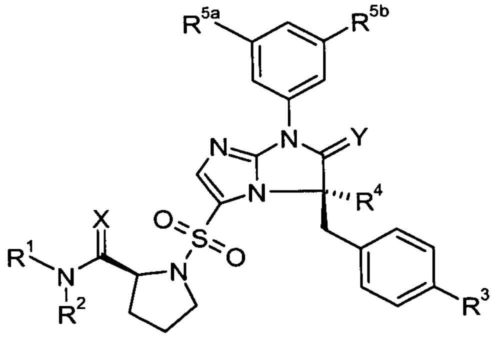
R^{5b} is Cl;

X is an oxygen atom; and

Y is an oxygen atom;

or a pharmaceutically acceptable salt thereof.

4. A compound of formula I according to claim 1 having the absolute stereochemistry depicted below by formula I*:



(I*).

5. ({(S)-1-[(R)-5-(4-Cyano-benzyl)-7-(3,5-dichloro-phenyl)-5-methyl-6-oxo-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carbonyl}-amino)-acetic acid.

6. ({(S)-1-[(R)-7-(3,5-Dichloro-phenyl)-5-methyl-6-oxo-5-(4-pyrimidin-5-yl-benzyl)-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carbonyl}-amino)-acetic acid.

7. (S)-1-[(R)-5-(4-Cyano-benzyl)-7-(3,5-dichloro-phenyl)-5-methyl-6-oxo-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid (2-hydroxy-2-methyl-propyl)-amide.

8. (S)-1-[(R)-5-(4-Cyano-benzyl)-7-(3,5-dichloro-phenyl)-5-methyl-6-oxo-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid (2-hydroxy-ethyl)-amide.

9. (S)-1-[(R)-5-(4-Cyano-benzyl)-7-(3,5-dichloro-phenyl)-5-methyl-6-oxo-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid carbamoylmethyl-amide.

10. (S)-1-[(R)-5-[4-(2-Cyano-pyridin-3-yl)-benzyl]-7-(3,5-dichloro-phenyl)-5-methyl-6-oxo-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid (2-hydroxy-2-methyl-propyl)-amide.

11. (S)-1-[(R)-5-[4-(2-Cyano-pyridin-3-yl)-benzyl]-7-(3,5-dichloro-phenyl)-5-methyl-6-oxo-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid carbamoylmethyl-amide.

12. (S)-1-[(R)-7-(3,5-Dichloro-phenyl)-5-methyl-6-oxo-5-(4-pyrimidin-5-yl-benzyl)-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid (1H-tetrazol-5-ylmethyl)-amide.

13. (S)-1-[(R)-7-(3,5-Dichloro-phenyl)-5-methyl-6-oxo-5-(4-trifluoromethoxy-benzyl)-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid (2-hydroxy-2-methyl-propyl)-amide.

14. (S)-1-[(R)-7-(3,5-Dichloro-phenyl)-5-methyl-6-oxo-5-(4-trifluoromethoxy-benzyl)-6,7-dihydro-5H-imidazo[1,2-a]imidazole-3-sulfonyl]-pyrrolidine-2-carboxylic acid carbamoylmethyl-amide.

15. A pharmaceutical composition comprising a compound in accordance with claim 1 and at least one pharmaceutically acceptable carrier, diluent or excipient.

16. A method for treating inflammation or an inflammatory condition in a patient which comprises administering to said patient a therapeutically effective amount of a compound in accordance with claim 1.

17. The method of claim 16 wherein the condition to be treated is adult respiratory distress syndrome, shock, oxygen toxicity, multiple organ injury syndrome secondary to septicemia, multiple organ injury syndrome secondary to trauma, reperfusion injury of tissue due to cardiopulmonary bypass, myocardial infarction or use with thrombolysis agents, acute glomerulonephritis, vasculitis, reactive arthritis, dermatosis with acute inflammatory components, stroke, thermal injury, hemodialysis, leukapheresis, ulcerative colitis, necrotizing enterocolitis or granulocyte transfusion associated syndrome.

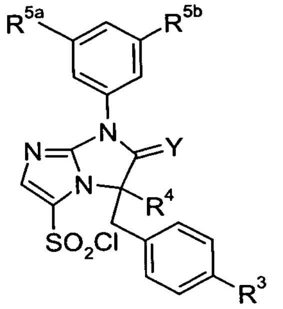
18. The method of claim 16 wherein the condition to be treated is psoriasis, organ/tissue transplant rejection, graft vs. host reaction or an autoimmune disease.

19. The method of claim 16 wherein the condition to be treated is Raynaud's syndrome, autoimmune thyroiditis, dermatitis, multiple sclerosis, rheumatoid arthritis, insulin-dependent diabetes mellitus, uveitis, inflammatory bowel disease, Crohn's disease, ulcerative colitis or systemic lupus erythematosus.

20. The method of claim 16 wherein the condition to be treated is asthma.

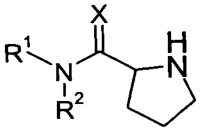
21. The method of claim 16 wherein the condition to be treated is the toxic effects of cytokine therapy.

22. A method for making a compound of the formula I according to claim 1, which method comprises reacting a compound of the formula IX



(IX)

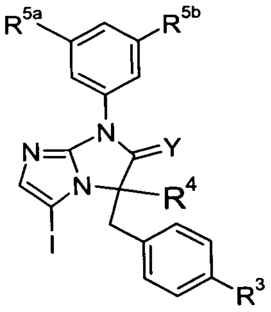
wherein R^3, R^4 , R^{5a} and R^{5b} and Y are as defined in claim 1, with a compound of the formula X



(X),

wherein R^1, R^2 and X are as defined in claim 1, to obtain a compound of the formula I.

23. A method according to claim 22, wherein the compound of formula IX is obtained by a method comprising reacting a compound of the formula II



(II),

wherein R^3, R^4 , R^{5a} and R^{5b} and Y are as defined in claim 22, with a Grignard reagent followed by treatment with SO_2 and *N*-chlorosuccinimide to obtain a compound of the formula IX.